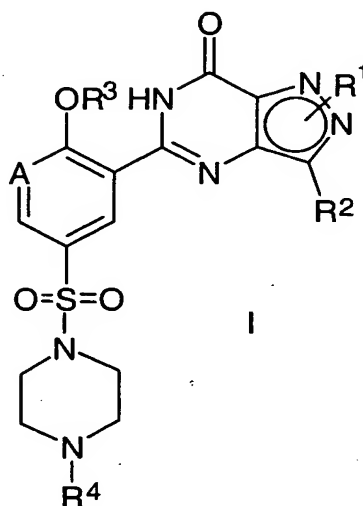


Claims

1. A process for the production of a compound of general formula I:



5

wherein

A represents CH or N;

R^1 represents H, lower alkyl (which alkyl group is optionally interrupted by
 10 O), Het, alkylHet, aryl or alkylaryl, which latter five groups are all
 optionally substituted (and/or, in the case of lower alkyl, optionally
 terminated) by one or more substituents selected from halo, cyano, nitro,
 lower alkyl, OR^5 , $C(O)R^6$, $C(O)OR^7$, $C(O)NR^8R^9$, $NR^{10a}R^{10b}$ and
 $SO_2NR^{11a}R^{11b}$;

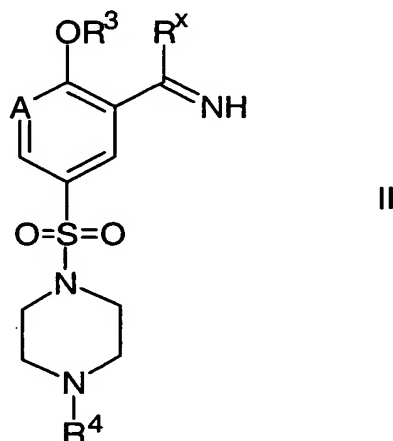
15 R^2 and R^4 independently represent lower alkyl;

R^3 represents lower alkyl, which alkyl group is optionally interrupted by
 oxygen;

Het represents an optionally substituted four- to twelve-membered
 heterocyclic group, which group contains one or more heteroatoms selected
 20 from nitrogen, oxygen and sulfur;

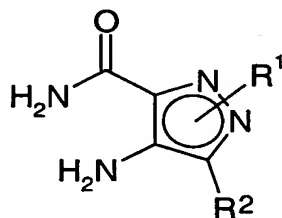
R^5 , R^6 , R^7 , R^8 , R^9 , R^{11a} and R^{11b} independently represent H or lower alkyl;
 R^{10a} and R^{10b} either independently represent, H or lower alkyl or, together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl or piperidinyl,

5 which process comprises the reaction of a compound of formula II,



wherein R^x is a group substitutable by an aminopyrazole and A, R^3 and R^4 are as defined above,
 with a compound of general formula III,

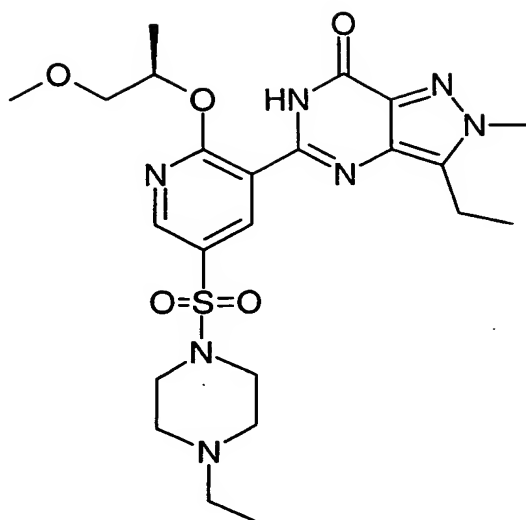
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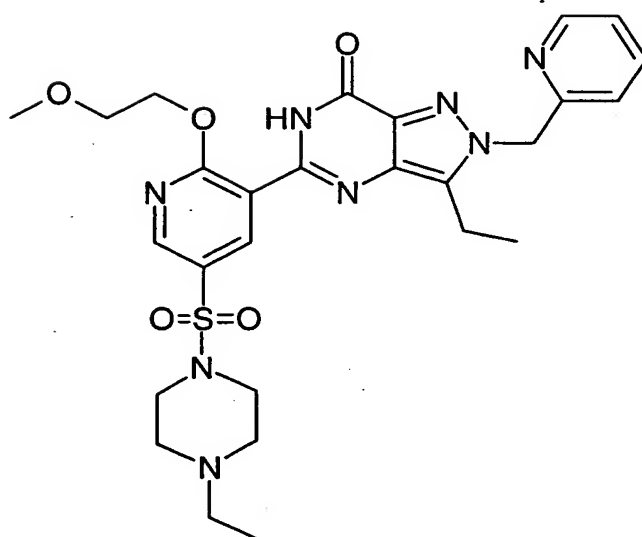
wherein R^1 and R^2 are as defined above.

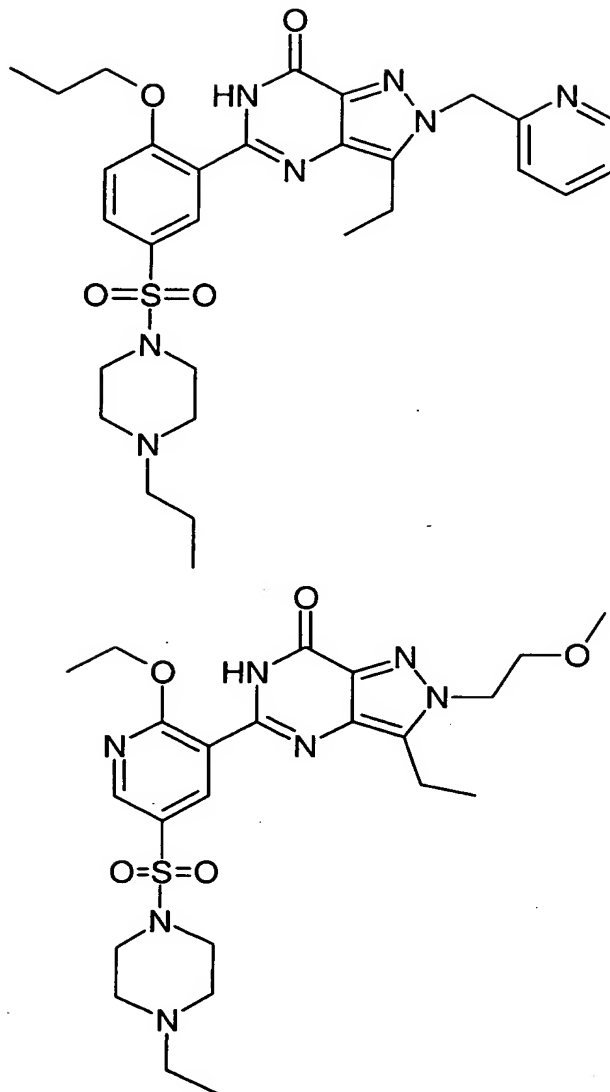
2. A process as claimed in Claim 1, wherein, in the compound of general
 15 formula I, R^1 represents C_{1-4} alkyl, which alkyl group is optionally interrupted by an oxygen atom, and/or is optionally terminated by a Het group.

3. A process as claimed in Claim 2, wherein R^1 represents linear C_{1-3} alkyl, which alkyl group is optionally interrupted by an oxygen atom, or is optionally terminated by a 2-pyridinyl group.
- 5 4. A process as claimed in any one of the preceding claims, wherein, in the compound of general formula I, R^2 represents C_{1-4} alkyl.
- 10 5. A process as claimed in Claim 4, wherein R^2 represents linear C_{2-3} alkyl.
6. A process as claimed in any one of the preceding claims, wherein, in the compound of general formula I, R^3 represents C_{1-5} alkyl, which alkyl group is optionally interrupted by an oxygen atom.
- 15 7. A process as claimed in Claim 6, wherein R^3 represents linear or branched C_{2-4} alkyl, which alkyl group is optionally interrupted by an oxygen atom.
- 20 8. A process as claimed in any one of the preceding claims, wherein, in the compound of general formula I, R^4 represents C_{1-3} alkyl.
9. A process as claimed in Claim 8, wherein R^4 represents C_{1-2} alkyl.
- 25 10. A process as claimed in any one of the preceding claims, wherein the compound is selected from sildenafil, or any one of the following four compounds



5





11. A process as claimed in any one of the preceding claims, wherein the
5 group R^x of the compound of formula II represents $-NH_2$, $-NHR^a$,
 $-N(R^b)R^c$, $-SR^d$, $-SH$, $-OR^e$ (in which groups R^a to R^e each independently
represent the same groups that R^1 as defined in Claim 1 may represent,
except that they do not represent H) or halo.

12. A process as claimed in Claim 11, wherein R^x represents $-NHR^a$, $-N(R^b)R^c$, $-SR^d$, $-SH$ or $-OR^e$.

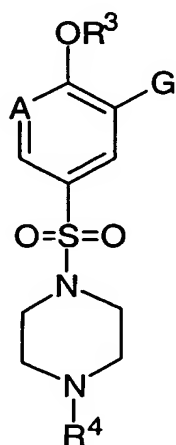
13. A process as claimed in Claim 12, wherein R^x represents ethoxy.

14. A process as claimed in any one of the preceding claims, wherein the reaction is carried out in the presence of a solvent system that includes an aromatic hydrocarbon, chlorobenzene or a solvent of formula R^xH , wherein R^x is as defined in any one of Claims 1 or 11 to 13.

15. A process as claimed in Claim 14, wherein the solvent is toluene, xylene, chlorobenzene or ethanol.

16. A process as claimed in Claim 14 or Claim 15, wherein the reaction is carried out at reflux temperature.

17. A process as claimed in any one of the preceding claims, wherein the compound of formula II is prepared by way of reaction of a compound of formula IV,



IV

wherein G represents a carboxylic acid group ($-C(O)OH$) or a derivative thereof, and A, R^3 and R^4 are as defined in any one of Claims 1 and 6 to 10

(as appropriate), with an appropriate reagent for converting the group G to a $-C(R^x)=NH$ group, wherein R^x is as defined in any one of Claims 1 or 11 to 13.

5 18. A process as claimed in Claim 17, wherein, in the compound of formula IV, the group G represents $-CN$, $-C(OR^e)_3$, $-C(O)NH_2$ or $-C(=NOR^f)NR_2$, wherein R^f represents H or lower alkyl and R^e is as defined in Claim 11.

10 19. A process as claimed in Claim 18, wherein, when R^x represents $-OR^e$ (wherein R^e represents lower alkyl (optionally interrupted by O), alkylHet or alkylaryl):

(a) a corresponding compound of formula IV in which G represents $-CN$ is reacted with an alcohol of formula VA,

15



wherein R_α represents lower alkyl (optionally interrupted by O), alkylHet or alkylaryl, and Het is as defined in Claim 1, in the presence of a protic acid;

(b) a corresponding compound of formula IV in which G represents $-C(O)NH_2$ is reacted with an appropriate alkylating agent of formula VB,

20



wherein Z^1 represents a leaving group and R_α is as defined above; or

(c) a corresponding compound of formula IV in which G represents $-C(OR_\alpha)_3$, wherein R_α is as defined above, is reacted with ammonia, or
25 an *N*-protected derivative thereof.

20. A process as claimed in Claim 18, wherein, when R^x represents $-OR^e$ (wherein R^e represents Het or aryl), a corresponding compound of formula IV in which G represents $-CN$ is reacted with a compound of formula VC,



5 wherein R_β represents Het or aryl, and Het is as defined in Claim 1.

21. A process as claimed in Claim 18, wherein, when R^x represents $-NH_2$:

- 10 (a) a corresponding compound of formula IV in which G represents $-CN$ is reacted with hydrazine, hydroxylamine or *O*-lower alkyl hydroxylamine, followed by reduction of the resultant intermediate under standard conditions; or
- (b) a corresponding compound of formula IV in which G represents $-C(=NOR^f)NR_2$, wherein R^f is as defined in Claim 18, is reduced under
- 15 standard conditions.

22. A process as claimed in Claim 18, wherein, when R^x represents $-NH_2$, $-NHR^a$ or $-N(R^b)R^c$, a corresponding compound of formula IV in which G represents $-CN$ is reacted with a compound of formula VD,

20



wherein R_χ and R_δ independently represent H or R^a , and R^a is as defined in Claim 11.

23. A process as claimed in Claim 18, wherein, when R^x represents $-SH$:

- 25 (a) a corresponding compound of formula IV in which G represents $-CN$ is reacted with hydrogen sulfide; or

(b) a corresponding compound of formula IV in which G represents $-C(O)NH_2$ is reacted with a reagent that effects oxygen-sulfur exchange.

- 5 24. A process as claimed in Claim 18, wherein, when R^x represents $-SR^d$, a corresponding compound of formula IV in which G represents $-CN$ is reacted with a compound of formula VE,



wherein R^d is as defined in Claim 11.

10

25. A process as claimed in Claim 18, wherein, when R^x represents halo, a corresponding compound of formula IV in which G represents $-C(O)NH_2$ is reacted with a halogenating agent.

- 15 26. A process as claimed in any one of Claims 1 to 16, wherein the compound of formula II is prepared by way of reaction of another compound of formula II with a reagent that will convert one R^x group to another, wherein R^x is as defined in any one of Claims 1 or 11 to 13.

- 20 27. A process as claimed in Claim 26, wherein, when R^x represents $-OR^e$ (wherein R^e represents lower alkyl, alkylHet or alkylaryl), a corresponding compound of formula II in which R^x represents Cl is reacted with a compound of formula VA, as defined in Claim 19.

- 25 28. A process as claimed in Claim 26, wherein, when R^x represents $-NH_2$, $-NHR^a$ or $-N(R^b)R^c$, a corresponding compound of formula II in which R^x represents Cl, $-SH$, $-SR^d$ or $-OR^e$, wherein R^d and R^e are as defined in Claim 11, is reacted with an appropriate compound of formula VD, as defined in Claim 22, or an acid addition salt thereof.

29. A process as claimed in Claim 26, wherein, when R^x represents $-SR^d$, a corresponding compound of formula IV in which R^x represents $-SH$ is reacted with a compound of formula VF,

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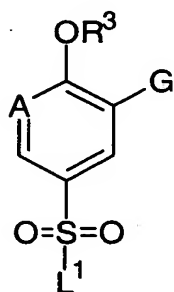


VF

wherein Z^2 represents a leaving group and R^d is as defined in Claim 11.

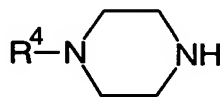
30. A process as claimed in any one of Claims 17 to 25, wherein the compound of formula IV is prepared by reaction of a compound of formula

10 VI,



VI

wherein L^1 is a leaving group and A, G and R^3 are as defined in any one of Claims 1, 6, 7, 10, 17 and 18 (as appropriate), with a compound of formula VII,

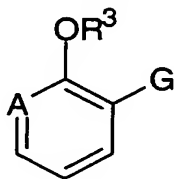


VII

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wherein R^4 is as defined in any one of Claims 1 and 8 to 10.

31. A process as claimed in Claim 30, wherein the compound of formula VI is prepared by reaction of a compound of formula VIII,

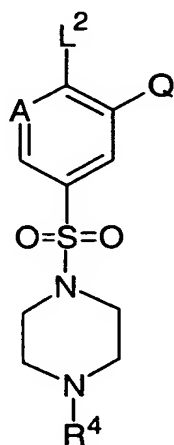


VIII

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wherein A, G and R³ are as defined in any one of Claims 1, 6, 7, 10, 17 and 18 (as appropriate), with a reagent that may be used for the introduction of a -SO₂L¹ group into an aromatic or heteroaromatic ring system.

- 5 32. A process as claimed in any one of Claims 17 to 24, wherein the compound of formula IV is one in which G represents -CN or -C(O)NH₂, and is prepared by reaction of a compound of formula IX,



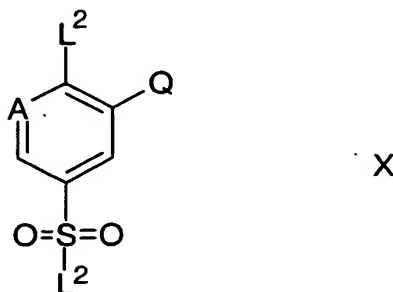
IX

- 10 wherein Q represents -CN or -C(O)NH₂, L² represents a leaving group and A and R⁴ are as defined in any one of Claims 1 and 8 to 10, with a compound that will provide the group R³O.

33. A process as claimed in Claim 32, wherein the compound that will
15 provide the group R³O is a lower alkyl alcohol.

34. A process as claimed in Claim 32 or 33, wherein the leaving group L² is chloro.

35. A process as claimed in any one of Claims 32 to 34, wherein the compound of formula IX is prepared by reaction of a compound of formula X,



5 wherein Q and L² are as defined in Claim 32, and A is as defined in Claim 1, with a compound of formula VII as defined in Claim 30.

36. A process as claimed in any one of Claims 17 to 24, wherein the compound of formula IV is one in which G represents -CN, and is prepared
10 by dehydration of a corresponding compound of formula IV in which G represents -C(O)NH₂.

37. A process as claimed in any one of Claims 17 to 19, 23 and 25, wherein the compound of formula IV in which G represents -C(O)NH₂ is
15 prepared from a corresponding compound of formula IV in which G represents -C(O)OH by reaction with ammonia or a derivative thereof.

38. A compound of formula II, as defined in any one of Claims 1 and 11 to
13.

20

39. A compound according to Claim 38 wherein A represents -CH, R³ represents Et, R⁴ represents Me and R^x represents NH₂.

40. A compound according to Claim 38 wherein A represents $-\text{CH}$, R^3 represents Et, R^4 represents Et and R^x represents NH_2 .
41. A compound of formula IV, as defined in Claim 17 or Claim 18.
- 5 42. A compound according to Claim 39 wherein A represents N, R^3 represents Et, R^4 represents Et and G represents CO_2H .
- 10 43. A compound according to Claim 39 wherein A represents N, R^3 represents Et, R^4 represents Et and G represents CO_2Et .
44. A compound according to Claim 39 wherein A represents $-\text{CH}$, R^3 represents Et, R^4 represents Et and G represents CN.
- 15 45. A compound according to Claim 39 wherein A represents $-\text{CH}$, R^3 represents Et, R^4 represents Me and G represents CN.